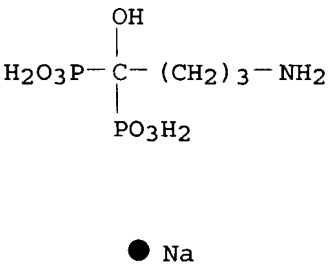
L16 ANSWER 1 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:88861 HCAPLUS
DOCUMENT NUMBER: 131:653
TITLE: Effect of alendronate on primary osteoporosis
AUTHOR(S): Meng, Xunwu; Zhu, Hanmin; Liu, Jianli; Zhang, Shaofen; Xia, Weibo; Chen, Xiaoping; Zhang, Zhonglan; Zhu, Zhiling; Yu, Wei; Chen, Shuying
CORPORATE SOURCE: Peking Union Medical College Hospital, Chinese Academy of Medical Science, Peking Union Medical College, Beijing, 100730, Peop. Rep. China
SOURCE: Zhonghua Neifenmi Daixie Zazhi (1998), 14(5), 295-298
CODEN: ZNDZEK; ISSN: 1000-6699
PUBLISHER: Shanghaishi Neifenmi Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

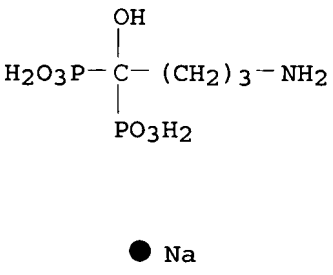
AB The efficiency and safety of alendronate (Fosamax) on primary osteoporosis were studied. This is a multi-center open-labeled study. Eighty-one Chinese women aged 65 ± 6 yr in average with primary osteoporosis were enrolled. The years since their menopause were 15 ± 6 yr. Seventy-nine, 76 and 70 women received alendronate 10 mg and calcium 500 mg daily for 3, 6 and 12 mo, resp. Follow-up dual energy x-ray absorptiometry showed that bone mineral d. (BMD) increased significantly in the lumbar spine (L2-4 by 2.8%, 4.1% and 6.3% in 3, 6 and 12 mo resp.). The BMD of L2-4 was higher in 6 mo than that of 3 mo after treatment, and even higher at 12 mo and thereafter. The hip BMD increased obviously 3, 6 and 12 mo after treatment. The increase was most significant (2.6%-2.9%) at the trochanter. The BMD of femoral neck and ward triangle rose after treatment, but no progressive increase was found during the 12 mo of treatment. The adverse effects probably associated with alendronate were found in 3 patients and were mainly mild abdominal symptoms. No serious adverse effects were observed Alendronate significantly increases the lumbar and hip BMD, and is well tolerated at a dose of 10 mg daily for a duration of 1 yr in the treatment of primary osteoporosis in Chinese women.

IT 129318-43-0, Fosamax
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alendronate effect on primary osteoporosis in postmenopausal Chinese women)
RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



L16 ANSWER 2 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:34189 HCAPLUS
DOCUMENT NUMBER: 130:218463
TITLE: Effect of alendronate on risk of fracture in women with low bone density but without vertebral fractures: Results from the fracture intervention trial

AUTHOR(S): Cummings, Steven R.; Black, Dennis M.; Thompson, Desmond E.; Applegate, William B.; Barrett-Connor, Elizabeth; Musliner, Thomas A.; Palermo, Lisa; Prineas, Ronald; Rubin, Susan M.; Scott, Jean C.; Vogt, Thomas; Wallace, Robert; Yates, A. John; LaCroix, Andrea Z.
CORPORATE SOURCE: Departments of Epidemiology and Biostatistics, University of California, San Francisco, CA, USA
SOURCE: JAMA, the Journal of the American Medical Association (1998), 280(24), 2077-2082
CODEN: JAMAAP; ISSN: 0098-7484
PUBLISHER: American Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Alendronate sodium reduces fracture risk in postmenopausal women who have vertebral fractures, but its effects on fracture risk have not been studied for women without vertebral fractures. The objective of this study was to test the hypothesis that 4 yr of alendronate would decrease the risk of clin. and vertebral fractures in women who have low bone mineral d. (BMD) but no vertebral fractures. Women aged 54 to 81 yr with a femoral neck BMD of 0.68 g/Cm2 or less, but no vertebral fracture, were randomized to alendronate or placebo groups. All participants reporting calcium intakes of 1000 mg/d or less received a supplement containing 500 mg of calcium and 250 IU of cholecalciferol. Subjects were randomly assigned to either placebo or 5 mg/d of alendronate sodium for 2 yr followed by 10 mg/d for the remainder of the trial. Clin. fractures confirmed by x-ray reports, new vertebral deformities detected by morphometric measurements on radiographs, and BMD measured by dual x-ray absorptiometry were analyzed. Alendronate increased BMD at all sites studied and reduced the incidence of clin. fractures by 14%. Alendronate reduced clin. fractures by 36% in women with baseline osteoporosis at the femoral neck, but there was no significant reduction among those with higher BMD. Alendronate decreased the risk of radiog. vertebral fractures by 44% overall. Alendronate did not increase the risk of gastrointestinal or other adverse effects. Thus, in women with low BMD but without vertebral fractures, 4 yr of alendronate safely increased BMD and decreased the risk of first vertebral deformity. Alendronate significantly reduced the risk of clin. fractures among women with osteoporosis but not among women with higher BMD.
IT 129318-43-0, Alendronate sodium
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alendronate effect on risk of fracture in women with low bone d. but without vertebral fractures)
RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

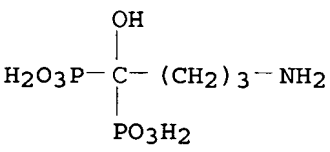
L16 ANSWER 3 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:21587 HCAPLUS
DOCUMENT NUMBER: 130:86172
TITLE: Effervescent alendronate formulation
INVENTOR(S): Katdare, Ashok V.; Kramer, Kenneth A.; Gardner, Colin R.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 4 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5853759	A	19981229	US 1997-848460	19970508 <--
US 2001041165	A1	20011115	US 2001-878557	20010611
US 2004137058	A1	20040715	US 2004-751791	20040105
US 2006034921	A1	20060216	US 2005-253392	20051019
US 2007087052	A1	20070419	US 2006-390114	20060327

PRIORITY APPLN. INFO.:

US 1996-17881P	P	19960517
US 1997-848460	A1	19970508
US 1998-50341	B1	19980330
US 2002-191669	A1	20020709
US 2004-751791	A1	20040105
US 2005-253392	A1	20051019

AB An effervescent formulation of alendronate contains an acid source, a carbonate source, a binder, a lubricant and optionally, flavoring agents, colorants and sweeteners. An effervescent tablet contained alendronate sodium 10 (as alendronic acid), citric acid 650, sodium bicarbonate 367, sodium carbonate 40, sodium benzoate 7.5, flavoring agents 25, colorants 5, and water 2 mg.
IT 129318-43-0, Alendronate sodium
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effervescent alendronate formulation)
RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:7805 HCAPLUS
DOCUMENT NUMBER: 130:71559
TITLE: Film-coated tablet for improved upper gastrointestinal tract safety
INVENTOR(S): Dansereau, Richard John; Bekker, Petrus Jakobus
PATENT ASSIGNEE(S): The Procter & Gamble Company, USA

SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

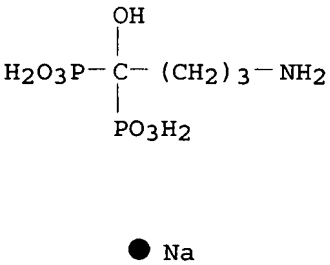
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9856360	A2	19981217	WO 1998-IB883	19980608 <--
WO 9856360	A3	19990311		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2293815	A1	19981217	CA 1998-2293815	19980608 <--
CA 2293815	C	20040629		
AU 9874460	A	19981230	AU 1998-74460	19980608 <--
AU 729912	B2	20010215		
EP 989848	A2	20000405	EP 1998-921690	19980608
EP 989848	B1	20040929		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
TR 200000111	T2	20000522	TR 2000-200000111	19980608
BR 9810027	A	20000912	BR 1998-10027	19980608
HU 200004625	A2	20010628	HU 2000-4625	19980608
JP 2002504112	T	20020205	JP 1999-501960	19980608
RU 2193880	C2	20021210	RU 2000-100940	19980608
NZ 503946	A	20030228	NZ 1998-503946	19980608
AT 277606	T	20041015	AT 1998-921690	19980608
PT 989848	T	20041231	PT 1998-921690	19980608
SG 108292	A1	20050128	SG 2002-200200225	19980608
ES 2226128	T3	20050316	ES 1998-921690	19980608
SK 284690	B6	20050908	SK 1999-1718	19980608
ZA 9805010	A	19990226	ZA 1998-5010	19980610
US 6165513	A	20001226	US 1998-95322	19980610
IN 1998DE01619	A	20061208	IN 1998-DE1619	19980611
TW 542725	B	20030721	TW 1998-87110727	19980702
NO 9906116	A	20000211	NO 1999-6116	19991210
MX 9911622	A	20010710	MX 1999-11622	19991213
HK 1028187	A1	20050520	HK 2000-106110	20000926
US 6569460	B1	20030527	US 2000-694799	20001023
US 2003211156	A1	20031113	US 2003-401352	20030328
US 2007071822	A1	20070329	US 2006-607241	20061201

PRIORITY APPLN. INFO.:

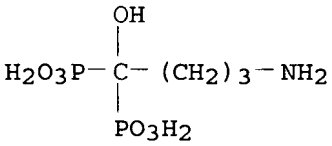
US 1997-49306P	P	19970611
WO 1998-IB883	W	19980608
US 1998-95322	A1	19980610
US 2000-694799	A3	20001023
US 2003-401352	B1	20030328

AB A novel oral dosage to be delivered to the stomach comprising a safe and effective amount of an active ingredient selected from the group consisting of emepronium bromide, doxycycline, and other tetracycline antibiotics, iron prepns., quinidine, nonsteroidal anti-inflammatory drugs, alprenolol, ascorbic acid, captopril, theophylline, zidovudine (AZT), bisphosphonates and mixts. thereof and pharmaceutically acceptable excipients, wherein said oral dosage form is a generally oval form and film coated to facilitate rapid esophageal transit and avoid irritation in the mouth, buccal cavity, pharynx, and esophagus. Film-coating with Dri-Klear (mixture of HPMC, hydroxypropyl cellulose, PEG, and silica) was applied to 110 kg of risedronate core tablets, each weighing 240 mg.

IT 129318-43-0, Alendronate sodium
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(film-coated tablet for improved upper gastrointestinal tract safety)
RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



L16 ANSWER 5 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:649801 HCAPLUS
DOCUMENT NUMBER: 130:61003
TITLE: Esophageal irritation due to alendronate sodium tablets, Possible mechanisms
AUTHOR(S): Peter, C. P.; Handt, L. K.; Smith, S. M.
CORPORATE SOURCE: Merck Research Laboratories, West Point, PA, 19486, USA
SOURCE: Digestive Diseases and Sciences (1998), 43(9), 1998-2002
CODEN: DDSCDJ; ISSN: 0163-2116
PUBLISHER: Plenum Publishing Corp.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Animal studies were done using an in vivo dog model to examine the possible mechanism for the esophageal adverse events reported with alendronate sodium tablets. These studies showed that under low pH conditions alendronate sodium can cause esophageal irritation. No esophageal irritation occurred at pH 3.5 or higher where the drug exists primarily as the sodium salt. The animal studies also showed that alendronate sodium can exacerbate preexisting esophageal damage. Exposure of the esophageal mucosa for a prolonged period to alendronate sodium tablet can also cause mild esophageal irritation. These findings suggest that the esophageal irritation in patients taking Fosamax can be from prolonged contact with the tablet, reflux of acidic gastric contents with alendronate sodium, and exacerbation of preexisting esophageal damage. The findings also suggest that other bisphosphonates can cause esophageal injury under similar conditions.
IT 129318-43-0, Alendronate sodium
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(esophageal irritation due to alendronate sodium tablets)
RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



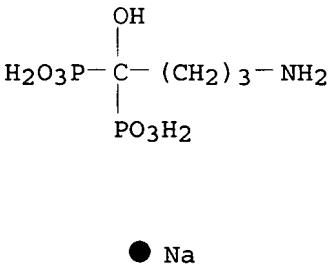
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:641102 HCAPLUS
DOCUMENT NUMBER: 130:10502
TITLE: Effects of incadronate and alendronate on the gastric mucosa in rats
AUTHOR(S): Yamano, Mayumi; Fujihara, Akira; Usuda, Shinji
CORPORATE SOURCE: Applied Pharmacology Lab., Inst. Drug Discovery Res., yamanouchi Pharmaceutical Co., Ltd., Ibaraki, 305-8585, Japan
SOURCE: Oyo Yakuri (1998), 56(1), 17-21
CODEN: OYYAA2; ISSN: 0300-8533
PUBLISHER: Oyo Yakuri Kenkyukai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Gastrotoxic effects of bisphosphonates, incadronate disodium (YM175) and alendronate sodium, were examined in rats. The effect of combined treatment of these bisphosphonates with indomethacin, a nonsteroidal anti-inflammatory drug (NSAID) on the gastric mucosa was also examined in rats. Daily oral treatment of incadronate (100 mg/kg) or alendronate (100 mg/kg) for 3 days significantly induced gastric mucosal lesion and hemorrhage, whereas lower doses (10-30 mg/kg) of them had no effect on the gastric mucosa. When incadronate (10-100 mg/kg p.o.) was administered with indomethacin (10 mg/kg s.c.) for 3 days, the gastric mucosal injury addnl. increased. However, this additive increase in the gastric mucosal injury was not significant. On the other hand, the combined treatment of alendronate (100 mg/kg p.o.) with indomethacin significantly enhanced the gastric mucosal lesion induced by indomethacin. These results suggest that repeated treatment of incadronate and alendronate at higher doses induced gastric mucosal injury in rats, and that gastrotoxic effect of incadronate is almost as potent as alendronate. It is also suggested that additive gastrotoxic effect may be observed when high doses of bisphosphonates therapy is combined with NSAID treatment in humans.

IT 129318-43-0, Alendronate sodium
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effects of incadronate and alendronate on the gastric mucosa in rats)

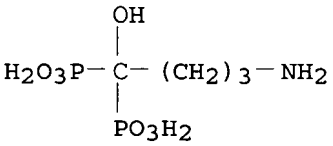
RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



L16 ANSWER 7 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:574148 HCAPLUS
DOCUMENT NUMBER: 129:339833
TITLE: Effects of alendronate sodium on severe osteodystrophy in postmenopausal patients with primary biliary cirrhosis: a pilot study
AUTHOR(S): Floreani, Annarosa; Tizian, Luisa; Luisetto, Giovanni; Buda, Andrea; Mega, Andrea; Naccarato, Remo
CORPORATE SOURCE: Department of Gastroenterology, University of Padova, Padua, 35100, Italy
SOURCE: Current Therapeutic Research (1998), 59(8), 589-593
CODEN: CTCEA9; ISSN: 0011-393X
PUBLISHER: Excerpta Medica
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Osteodystrophy is a major complication in primary biliary cirrhosis (PBC) and a significant problem for patients who require a liver transplant. Treatment for osteodystrophy has yet to be standardized. The goal of this pilot study was to assess the efficacy and tolerability of alendronate sodium, a potent specific inhibitor of osteoclast-mediated bone resorption. The study comprised 15 postmenopausal PBC patients (mean age, 64.25 ± 8.77 yr) with severe osteodystrophy. Four patients had histol. stage II disease, 8 stage III, and 3 stage IV. All patients had a T score below 2, indicating a fracture risk of 60%. All patients received two courses of alendronate sodium (10 mg/d for 3 mo, separated by a 2-mo interval). The following variables were assessed at baseline and after 10 mo: bone mineral d. (BMD) (by dual-energy x-ray absorptiometry in the lumbar spine), calcium, sodium, potassium, creatinine, 25-hydroxyvitamin D, parathyroid hormone, and osteocalcin. No patients dropped out of the study, and therapy was well tolerated by all patients. At the end of treatment, BMD increased significantly compared with baseline (0.714 ± 0.115 g/cm2 vs 0.740 ± 0.108 g/cm2). Although not statistically significant, a trend toward an increase in serum osteocalcin levels (1.4 ± 1.5 ng/mL vs 2.6 ± 1.4 ng/mL) was evident. These preliminary findings suggest that alendronate sodium may be helpful in treating severe osteodystrophy in postmenopausal patients with PBC. Larger, controlled trials using long-term treatment with alendronate sodium are needed to establish the efficacy and safety of this drug.

IT 129318-43-0, Alendronate sodium
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of alendronate sodium on severe osteodystrophy in postmenopausal humans with primary biliary cirrhosis)
RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



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REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 8 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:550428 HCAPLUS
DOCUMENT NUMBER: 129:149100
TITLE: Process for the production of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid or salts thereof
INVENTOR(S): Kubela, Rudolf; Tao, Yong
PATENT ASSIGNEE(S): Apotex Inc., Can.
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

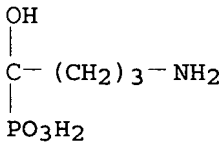
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9834940	A1	19980813	WO 1998-CA91	19980206 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2197267	A1	19980811	CA 1997-2197267	19970211 <--
CA 2197267	C	20000208		
AU 9859772	A	19980826	AU 1998-59772	19980206 <--
AU 728164	B2	20010104		
US 5908959	A	19990601	US 1998-19806	19980206
EP 971938	A1	20000119	EP 1998-902890	19980206
EP 971938	B1	20020710		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9807568	A	20000321	BR 1998-7568	19980206
AT 220404	T	20020715	AT 1998-902890	19980206
PT 971938	T	20021129	PT 1998-902890	19980206
ES 2180141	T3	20030201	ES 1998-902890	19980206

PRIORITY APPLN. INFO.: CA 1997-2197267 A 19970211
WO 1998-CA91 W 19980206
OTHER SOURCE(S): CASREACT 129:149100

AB A process is provided for the preparation of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid or salts thereof which comprises: (a) reacting 4-aminobutyric acid with phosphorous acid and phosphorus trichloride in the presence of a polyalkylene(glycol); and (b) recovering said 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid.

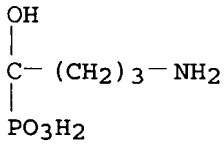
IT 129318-43-0P
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)
RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:431846 HCAPLUS
DOCUMENT NUMBER: 129:175699
TITLE: Synthesis and characterization of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid monosodium salt trihydrate
AUTHOR(S): Hu, Mingyang; Wang, Bocheng; Liang, Gaolin; Yang, Min
CORPORATE SOURCE: State Key Lab. Nucl. Med., Jiangsu Inst. Nucl. Med., Wuxi, 214063, Peop. Rep. China
SOURCE: Huaxue Shiji (1998), 20(2), 104-105
CODEN: HUSHDR; ISSN: 0258-3283
PUBLISHER: Huagongbu Huaxue Shiji Keji Qingbao Zhongxinzhan
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB This paper reports the synthesis of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid monosodium salt trihydrate (Aldronate). The structure has been characterized by elemental anal., MS, IR, and 1HNMR spectra.
IT 129318-43-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



L16 ANSWER 10 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:402324 HCAPLUS
DOCUMENT NUMBER: 129:72215
TITLE: Pharmaceutical compositions containing alendronate and gastric emptying promoting agent
INVENTOR(S): Fuisz, Richard C.

PATENT ASSIGNEE(S): Fuisz Technologies Ltd., USA
SOURCE: PCT Int. Appl., 8 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

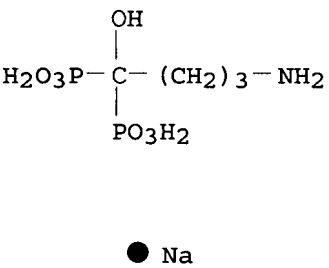
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9825628	A1	19980618	WO 1997-US22554	19971208 <--
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5773429	A	19980630	US 1996-762672	19961211 <--
CA 2250221	A1	19980618	CA 1997-2250221	19971208 <--
EP 938319	A1	19990901	EP 1997-950904	19971208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, IE				
JP 2001508769	T	20010703	JP 1998-526893	19971208

PRIORITY APPLN. INFO.: US 1996-762672 A 19961211
WO 1997-US22554 W 19971208

AB This invention encompasses a pharmaceutical composition comprising an effective amount of alendronate salt for reducing calcium loss and an effective amount of a gastric propulsive agent, preferably cisapride, to prevent gastric reflux caused by the alendronate salt. Thus a tablet contains alendronate sodium 10, cisapride 10 mg and other carriers such as celluloses, lactose and Mg stearate.

IT 129318-43-0, Alendronate sodium
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing alendronate and gastric emptying promoting agent)

RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



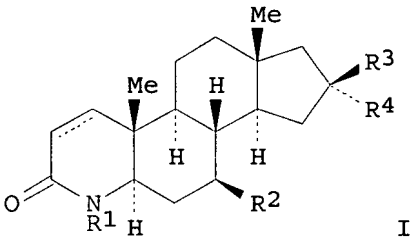
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 11 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:402269 HCAPLUS
DOCUMENT NUMBER: 129:86008
TITLE: Methods and compositions for preventing and treating bone loss
INVENTOR(S): Fuh, Vivian L.; Kaufman, Keith D.; Waldstreicher, Joanne
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9825463	A1	19980618	WO 1997-US22045	19971205 <--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5945412	A	19990831	US 1997-984425	19971203
AU 9853691	A	19980703	AU 1998-53691	19971205 <--
PRIORITY APPLN. INFO.:			US 1996-32634P	P 19961209
			GB 1997-293	A 19970108
			WO 1997-US22045	W 19971205

OTHER SOURCE(S): MARPAT 129:86008

GI



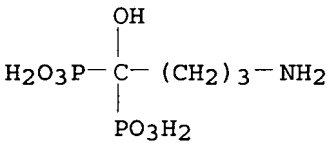
I

AB The present invention provides for a method of inhibiting bone loss in a subject in need of such treatment comprising administration to the subject of a therapeutically effective amount of an androstane I [R1, R2 = H, alkyl; one of R3 and R4 = H, Me, the other = NH2, CN, F, Me, carbamoyl, (un)substituted OH, SH, CHO,CO2H, acylamino, carbamoyloxy, ureido; R3R4 = O, alkylene]. Formulations containing 3-oxo-4-aza-7-methyl-16β-(4-methylphenoxy)-5α-androst-1-ene, 3-oxo-4-aza-4,7β-dimethyl-16β-phenoxy-5α-androstane, and 3-oxo-4-aza-4,7β-dimethyl-16β-(4-chlorophenoxy)-5α-androstane and, optionally, a growth hormone secretagogue, an estrogen, a bisphosphonate, or an antriestrogenic antiresorptive agent, are described.

IT 129318-43-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(azaandrostanone compns. for preventing and treating bone loss)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)

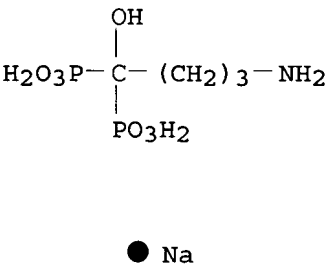


● Na

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 12 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:379760 HCAPLUS
DOCUMENT NUMBER: 129:202991
TITLE: Synthesis of alendronate sodium
AUTHOR(S): Jiao, Jian-Yu; Feng, Yi-Min; Shi, Shou-Yong; Xing, Yu-Ren
CORPORATE SOURCE: Shandong Institute Pharmaceutical Industry, Jinan, 250100, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (1998), 29(5), 202-203
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Alendronate sodium was prepared by treating 4-aminobutyric acid with phosphorous acid in chlorobenzene containing PCl3 followed by hydrolysis and treatment with aqueous NaOH.
IT 129318-43-0P, Alendronate sodium
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of alendronate sodium)
RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



● Na

L16 ANSWER 13 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:219721 HCAPLUS
DOCUMENT NUMBER: 128:299536
TITLE: Liquid alendronate formulations
INVENTOR(S): Nerurkar, Maneesh J.; Hunke, William H.; Ostovic, Drazen
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Nerurkar, Maneesh J.; Hunke, William H.; Ostovic, Drazen
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9814196	A1	19980409	WO 1997-US15740	19971002 <--

W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,

GN, ML, MR, NE, SN, TD, TG

CA 2267370	A1	19980409	CA 1997-2267370	19971002 <--
AU 9746448	A	19980424	AU 1997-46448	19971002 <--
AU 723357	B2	20000824		
BR 9712197	A	19990831	BR 1997-12197	19971002
CN 1238691	A	19991215	CN 1997-180165	19971002
EP 1007054	A1	20000614	EP 1997-945195	19971002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
HU 200000125	A2	20000628	HU 2000-125	19971002
HU 200000125	A3	20010428		
NZ 334836	A	20001124	NZ 1997-334836	19971002
JP 2001501222	T	20010130	JP 1998-516541	19971002
EE 3669	B1	20020415	EE 1999-113	19971002
NO 9901569	A	19990604	NO 1999-1569	19990330
KR 2000048829	A	20000725	KR 1999-702825	19990401

PRIORITY APPLN. INFO.:

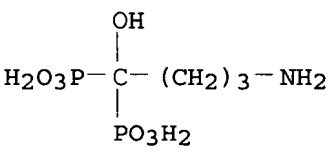
US 1996-26765P	P	19961004
GB 1997-541	A	19970113
US 1997-36002P	P	19970122
WO 1997-US15740	W	19971002

AB A liquid formulation of alendronic acid, or its salt has enough buffer so that the pH of the formulation is 4-7.5, and 15 mL of the formulation is able to raise the pH of 50 mL 0.1N HCl from 1 to 4. Thus, a formulation contained monosodium alendronate trihydrate 0.87, potassium sorbate 1.3, xylitol 400, sodium citrate dihydrate 100, and anhydrous citric acid 0.45 mg and water qs to 1 mL.

IT 129318-43-0, Monosodium Alendronate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid alendronate formulations)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 14 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:95237 HCAPLUS
DOCUMENT NUMBER: 128:115081
TITLE: Preparation of amino-diphosphinic acid and its sodium salts as bone absorption inhibitors
INVENTOR(S): Su, Guoqiang; Zhu, Chongquan; Bian, Jun
PATENT ASSIGNEE(S): Nanjing Pharmaceuticals Inst., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 6 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

CN 1144806	A	19970312	CN 1996-117031	19960725 <--
PRIORITY APPLN. INFO.:			CN 1996-117031	19960725

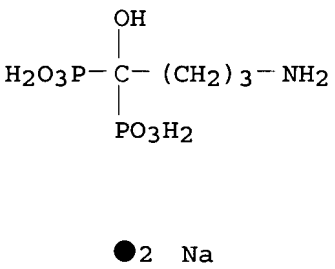
OTHER SOURCE(S): CASREACT 128:115081

AB Characterized is a process for preparation of the title compds. (I) by reacting PCl3 with aminocarboxylic acid in C6H5Cl. I are useful as bone absorption inhibitors (no data). Thus, H2N(CH2)2CO2H was reacted with PCl3 in C6H5Cl and followed by treatment with aqueous NaOH to give the title compound H2N(CH2)2COH(PO3HNa)2.

IT 134606-40-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino-diphosphinic acid and its sodium salts as bone absorption inhibitors)

RN 134606-40-9 HCAPLUS

CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



L16 ANSWER 15 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:731198 HCAPLUS

DOCUMENT NUMBER: 128:66563

TITLE: Analysis of selected diphosphonic acid derivatives used in treatment of osteoporosis. Part 1. Complexometric determination of diphosphonic acid derivatives

AUTHOR(S): Podolska, Marzena; Bialecka, Wanda; Kwiatkowska-Puchniarz, Barbara; Tuszynska, Ewa

CORPORATE SOURCE: Drug Institute, Warsaw, 00-725, Pol.

SOURCE: Acta Poloniae Pharmaceutica (1997), 54(4), 267-272
CODEN: APPHAX; ISSN: 0001-6837

PUBLISHER: Polish Pharmaceutical Society

DOCUMENT TYPE: Journal

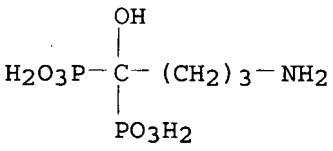
LANGUAGE: English

AB The purpose of the study was to develop a simple method for determination of diphosphonic acid derivs. in pharmaceutical prepns. used in treatment of osteoporosis: disodium etidronate, disodium clodronate, disodium tiludronate, disodium pamidronate, sodium alendronate. The anal. performed by the visual end point titration method with complexing reagent Th(DCTA) in presence of xylenol orange used the ability of these compds. to form complexes.

IT 129318-43-0, Fosamax
RL: ANT (Analyte); ANST (Analytical study)
(anal. of selected diphosphonic acid derivs. used in treatment of osteoporosis using complexometric titration)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



● Na

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 16 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:557645 HCAPLUS
DOCUMENT NUMBER: 127:239119
TITLE: Topical bisphosphonates for prevention of bone resorption
INVENTOR(S): Binderman, Itzhak; Yaffe, Avinoam
PATENT ASSIGNEE(S): Binderman, Itzhak, Israel; Yaffe, Avinoam
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729754	A1	19970821	WO 1997-IL50	19970212 <--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2245793	A1	19970821	CA 1997-2245793	19970212 <--
AU 9716161	A	19970902	AU 1997-16161	19970212 <--
AU 723516	B2	20000831		
EP 886521	A1	19981230	EP 1997-902554	19970212 <--
EP 886521	B1	20030521		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000504718	T	20000418	JP 1997-529156	19970212
AT 240737	T	20030615	AT 1997-902554	19970212
ES 2197329	T3	20040101	ES 1997-902554	19970212
HK 1016067	A1	20031017	HK 1999-101081	19990316
US 2002107228	A1	20020808	US 2002-108066	20020327

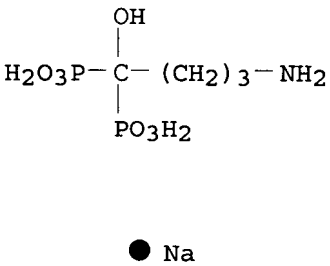
PRIORITY APPLN. INFO.:		
US 1996-11632P	P	19960214
GB 1996-3125	A	19960215
WO 1997-IL50	W	19970212
US 2000-572206	A1	20000517

AB Bisphosphonates inhibit bone resorption associated with periodontal or orthopedic surgery when applied topically to the bone. A novel formulation for topical application contains a gelatin matrix which is soaked in a solution containing a bone absorption inhibiting effective amount of a bisphosphonate or a pharmaceutically acceptable salt. A mucoperiosteal flap was made on both buccal and lingual aspect in the region of premolars and molars on both sides of the mandible, two quadrants per anesthetized rats. A 1 mm diameter piece of Gelfoam soaked in 0.025 mL of 20 g/L alendronate in saline solution was applied to the alveolar bone on both

buccal and lingual aspects on the exptl. (right) side and the flap was then preadapted immediately in place without suture. Gelfoam pellet lacking alendronate was applied to the alveolar bone in the the controls (left) side. Rats were sacrificed 21 days after surgery and high resolution X-ray microradiog. anal. was performed to show a typical resorption of alveolar bone specifically on the crest and its periodontal ligament aspect resulted in excessive alveolar bone loss, while on the exptl. side bone resorption was inhibited.

IT 129318-43-0, Alendronate sodium
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical bisphosphonates for prevention of bone resorption)

RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



L16 ANSWER 17 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:329299 HCAPLUS
DOCUMENT NUMBER: 126:301799
TITLE: Administration of alkalizing potassium salts and bisphosphonates for treatment of osteoporosis
INVENTOR(S): Marder, Herman L.; Morris, R. Curtis, Jr.; Sebastian, Anthony
PATENT ASSIGNEE(S): Regents of the University of California, USA; Marder, Herman L.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9712620	A1	19970410	WO 1996-US15594		19960927 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI					
AU 9673792	A	19970428	AU 1996-73792		19960927 <--
ZA 9608383	A	19970801	ZA 1996-8383		19961004 <--
IN 1996MA01757	A	20050304	IN 1996-MA1757		19961004
PRIORITY APPLN. INFO.:			US 1995-5397P	P	19951005
			US 1996-649039	A	19960516
			WO 1996-US15594	W	19960927

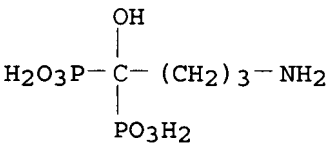
OTHER SOURCE(S): MARPAT 126:301799
AB The combination of the following active agents; (a) an alkalizing

potassium salt which produces hydroxyl ions and is thereby capable of reducing the acidity of tissue fluids or urine and which is selected from the group consisting of KHCO3 and potassium salts of carboxylic acids which are metabolized to bicarbonate and thus alkalinize in vivo and (b) a bisphosphonate which is effective as an antiresorptive agent for bone, is administered in amts. effective to treat osteoporosis without adversely affecting bone and acid-base homeostasis. As a protocol, a tablet containing 10 mg alendronate sodium was administered to a patient one hour before breakfast and two tablets each containing 1.5 g KHCO3 were administered concurrent with each of breakfast and dinner. This protocol was maintained for an extended period for chronic treatment of osteoporosis.

IT 129318-43-0, Alendronate sodium
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkalizing potassium salts and bisphosphonates for treatment of osteoporosis)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



L16 ANSWER 18 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:263931 HCAPLUS

DOCUMENT NUMBER: 126:312229

TITLE: Prevention of nonvertebral fractures by alendronate: a meta-analysis

AUTHOR(S): Karpf, David B.; Shapiro, Deborah R.; Seeman, Ego; Ensrud, Kristine E.; Johnston, C. Conrad, Jr.; Adami, Silvano; Harris, Steven T.; Santora, Arthur C., II; Hirsch, Laurence J.; Oppenheimer, Leonard; Thompson, Desmond

CORPORATE SOURCE: Merck Research Laboratories, Rahway, NJ, 07065-0900, USA

SOURCE: JAMA, the Journal of the American Medical Association (1997), 277(14), 1159-1164
CODEN: JAMAAP; ISSN: 0098-7484

PUBLISHER: American Medical Association

DOCUMENT TYPE: Journal

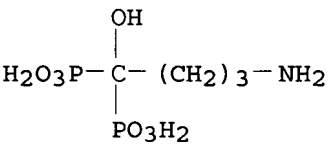
LANGUAGE: English

AB The purpose of this study is to evaluate the effect of treatment with alendronate sodium, a potent aminobisphosphonate, on the incidence of nonvertebral fractures in postmenopausal women with osteoporosis. All subjects were women with osteoporosis between the ages of 42 and 85 yr, postmenopausal at least 4 yr, with lumbar spine bone mineral d. (measured using dual-energy x-ray absorptiometry) at least 2.0 SD below the mean for young adult women. All women randomized to treatment with placebo or alendronate at a dose higher than 1 mg per day for at least 2 yr were included. In the placebo group (n=590), 60 women reported nonvertebral fractures during 1347 patient-years at risk (overall rate, 4.45 women with fractures per 100 patient-years at risk). In the alendronate group

(n=1012), 73 women reported nonvertebral fractures during 2240 patient-years at risk (overall rate, 3.26 women with fractures per 100 patient-years at risk). The estimated cumulative incidence of nonvertebral fractures after 3 yr was 12.6% in the placebo group and 9.0% in alendronate group. The relative risk for nonvertebral fracture estimated using the Cox proportional hazards model was 0.71 (95% confidence interval, 0.502-0.997) (P=.048). A reduction in risk was consistent across each of the studies and at each major site of osteoporotic fracture, including the hip and wrist. In postmenopausal women with osteoporosis, treatment with alendronate reduces the risk of nonvertebral fractures over at least 3 yr.

IT 129318-43-0, Alendronate sodium
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prevention of nonvertebral fractures by alendronate dealing with a meta-anal. in humans)

RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



● Na

L16 ANSWER 19 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:105205 HCAPLUS
DOCUMENT NUMBER: 126:122508
TITLE: Bisphosphonate cement composition to prevent aseptic loosening of orthopedic implant devices
INVENTOR(S): Simpson, Hamish; Athanasou, Nick; Yates, Ashley J.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA; Simpson, Hamish; Athanasou, Nick; Yates, Ashley J.
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9639107	A1	19961212	WO 1996-US8515	19960603 <--
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN				
RW: KE, LA, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2223450	A1	19961212	CA 1996-2223450	19960603 <--
AU 9659734	A	19961224	AU 1996-59734	19960603 <--
EP 831756	A1	19980401	EP 1996-917041	19960603 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11511041	T	19990928	JP 1996-501089	19960603

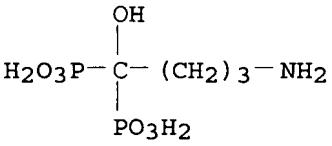
PRIORITY APPLN. INFO.: US 1995-470404 A 19950606
WO 1996-US8515 W 19960603

AB Disclosed is a bisphosphonate bone cement for preventing peri-prosthetic bone loss and aseptic loosening of a joint prosthesis in patients, which cement contains a bisphosphonate bone resorption inhibitor, e.g. Na or Ca salt of alendronate and a pharmaceutically acceptable polymeric carrier such as poly(Me methacrylate). A composition containing Me methacrylate, N,N-dimethyl-p-toluidine, and chlorophyll was added to a composition containing Me methacrylate-Me acrylate copolymer, benzoyl peroxide, ZrO2, chlorophyll, and gentamicin, then alendronate Na was added to give a cement mixture

IT 185959-98-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bone implant cements containing bisphosphonate bone resorption inhibitor and polymeric carrier)

RN 185959-98-2 HCAPLUS

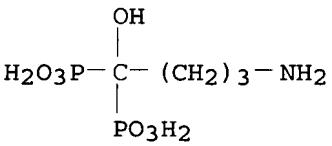
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, monohydrate (9CI) (CA INDEX NAME)



IT 129318-43-0, Alendronate sodium
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone implant cements containing bisphosphonate bone resorption inhibitor and polymeric carrier)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



L16 ANSWER 20 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:97191 HCAPLUS
DOCUMENT NUMBER: 126:108930
TITLE: Anhydrous monosodium alendronate formulations
INVENTOR(S): Brenner, Gerald S.; Ostovic, Drazen; Oberholtzer, Earl

R., Jr.; Thies, J. Eric
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

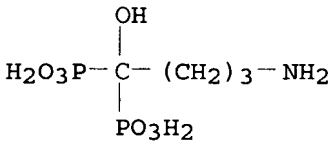
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9639149	A1	19961212	WO 1996-US8284	19960603 <--
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2221417	A1	19961212	CA 1996-2221417	19960603 <--
CA 2221417	C	20020430		
AU 9658860	A	19961224	AU 1996-58860	19960603 <--
EP 833643	A1	19980408	EP 1996-920607	19960603 <--
EP 833643	B1	20050216		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11506116	T	19990602	JP 1997-500937	19960603
JP 3344726	B2	20021119		
AT 289199	T	20050315	AT 1996-920607	19960603
PT 833643	T	20050630	PT 1996-920607	19960603
ES 2236737	T3	20050716	ES 1996-920607	19960603
US 5849726	A	19981215	US 1997-973386	19971203 <--

PRIORITY APPLN. INFO.: US 1995-469143 A1 19950606
WO 1996-US8284 W 19960603

AB A method for treating and prevention bone loss in patients by administering a formulation of anhydrous monosodium alendronate is described. Thus, alendronic acid was converted to the monosodium salt by treatment with 0.5N NaOH solution

IT 129318-43-0P, Monosodium alendronate
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anhydrous monosodium alendronate formulations)

RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



● Na

L16 ANSWER 21 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:94095 HCAPLUS
DOCUMENT NUMBER: 126:108945
TITLE: Disodium alendronate formulations
INVENTOR(S): Brenner, Gerald S.; Oberholtzer, Earl R., Jr.; Thies,

	J. Eric
PATENT ASSIGNEE(S):	Merck and Co., Inc., USA
SOURCE:	PCT Int. Appl., 9 pp.
	CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

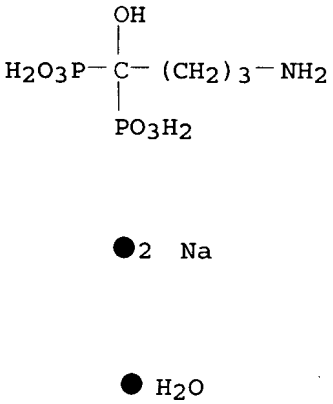
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9639410	A1	19961212	WO 1996-US8399	19960603 <--
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2221844	A1	19961212	CA 1996-2221844	19960603 <--
AU 9661483	A	19961224	AU 1996-61483	19960603 <--
EP 837863	A1	19980429	EP 1996-919036	19960603 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11506757	T	19990615	JP 1997-501011	19960603
US 2001021705	A1	20010913	US 2001-841126	20010424
PRIORITY APPLN. INFO.:			US 1995-469142 A1	19950606
			WO 1996-US8399 W	19960603
			US 1997-973384 A1	19971203
			US 2000-476274 A1	20000103

AB A method for treating and preventing bone loss in patients by administering a formulation of disodium alendronate, or its hydrates and formulations is described. Thus, alendronic acid was treated with 0.5N NaOH to give disodium salt monohydrate. The solubility of this salt was 200 mg/mL.

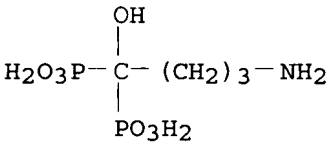
IT 185959-98-2P, Disodium Alendronate monohydrate
185959-99-3P, Disodium Alendronate pentahydrate
185960-00-3P, Disodium Alendronate trihydrate 185960-02-5P
, Disodium Alendronate hemihydrate
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(disodium alendronate formulations)

RN 185959-98-2 HCAPLUS

CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, monohydrate (9CI) (CA INDEX NAME)



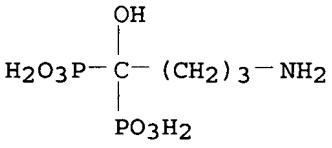
RN 185959-99-3 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, pentahydrate (9CI) (CA INDEX NAME)



●2 Na

●5 H_2O

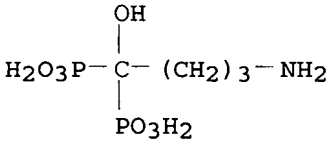
RN 185960-00-3 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, trihydrate (9CI) (CA INDEX NAME)



●2 Na

●3 H_2O

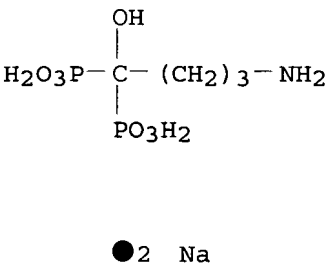
RN 185960-02-5 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, hydrate (2:1) (9CI) (CA INDEX NAME)



●2 Na

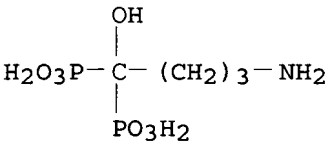
●1/2 H_2O

IT 134606-40-9P, Disodium Alendronate
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(disodium alendronate formulations)
RN 134606-40-9 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



L16 ANSWER 22 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:44943 HCAPLUS
DOCUMENT NUMBER: 126:152253
TITLE: Oncologic, endocrine & metabolic Alendronate (Fosamax): clinical utility in metabolic bone disease
AUTHOR(S): Hayes, Joathan; Sambrook, Philip
CORPORATE SOURCE: Garvin Inst. Med. Res., St. Vincent's Hosp, Sydney, Australia
SOURCE: Expert Opinion on Investigational Drugs (1996), 5(12), 1691-1705
CODEN: EOIDER; ISSN: 0967-8298
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 80 refs. Alendronate is a member of the class of drugs known as bisphosphonates, potent inhibitors of bone resorption which act via inhibition of osteoclast function. Unlike first generation bisphosphonates, alendronate does not appear to have deleterious effects on bond mineralizations at doses which inhibit bone resorption. Bisphosphonates have been studied in the management of a broad range of skeletal disorders characterized by increased bone turnover, including hypercalcemia of malignancy, metastatic bond disease, primary and secondary hyperparathyroidism, and Paget's disease of bone. More recently, bisphosphonates have also been studied in the prevention and treatment of established bone loss in patients with osteoporosis. In this respect, alendronate has recently been shown to increase bone mass in the spine, femoral neck and total body of postmenopausal women with osteoporosis, and to reduce the incidence of vertebral, hip and wrist fractures, the progression of vertebral deformities and height loss in these subjects. The drug appears to be safe and well tolerated apart from a low incidence of chemical esophagitis. Alendronate therefore offers a promising alternative to hormone replacement therapy for treatment of osteoporosis in postmenopausal women and may also may play a role in the management of other types of osteoporosis.
IT 129318-43-0, Fosamax
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(oncol. and endocrine alendronate (Fosamax) in metabolic bone disease treatment)
RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1)

(CA INDEX NAME)



● Na

REFERENCE COUNT: 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 23 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:175678 HCAPLUS
DOCUMENT NUMBER: 124:212066
TITLE: Pharmaceutical compositions containing a bisphosphonate and an anti-resorptive agent for inhibiting bone loss
INVENTOR(S): Black, Larry John; Cullinan, George Joseph
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
EP 693285	A2	19960124	EP 1995-305083	19950720	<--
EP 693285	A3	19980506			
EP 693285	B1	20020206			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
IN 1995CA00639	A	20050304	IN 1995-CA639	19950605	
ZA 9506029	A	19970120	ZA 1995-6029	19950719	<--
NZ 272608	A	20000526	NZ 1995-272608	19950719	
TW 398975	B	20000721	TW 1995-84107488	19950719	
PL 181304	B1	20010731	PL 1995-309693	19950719	
NO 9502890	A	19960123	NO 1995-2890	19950720	<--
NO 308194	B1	20000814			
AU 9527112	A	19960201	AU 1995-27112	19950720	<--
AU 693235	B2	19980625			
HU 72754	A2	19960528	HU 1995-2193	19950720	<--
RU 2149631	C1	20000527	RU 1995-114385	19950720	
IL 114683	A	20010614	IL 1995-114683	19950720	
AT 212846	T	20020215	AT 1995-305083	19950720	
ES 2168336	T3	20020616	ES 1995-305083	19950720	
PT 693285	T	20020628	PT 1995-305083	19950720	
CA 2154414	A1	19960123	CA 1995-2154414	19950721	<--
JP 08040911	A	19960213	JP 1995-185512	19950721	<--
BR 9503406	A	19960227	BR 1995-3406	19950721	<--
CN 1119940	A	19960410	CN 1995-108916	19950721	<--
CN 1079671	B	20020227			
US 2001051636	A1	20011213	US 2000-520737	20000308	
PRIORITY APPLN. INFO.:			US 1994-279363 A	19940722	

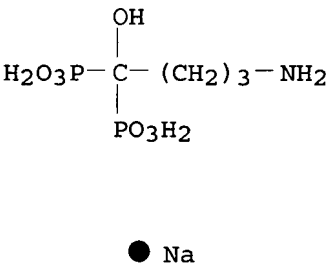
OTHER SOURCE(S): MARPAT 124:212066
AB A method for inhibiting bone loss comprises administering to a human in need thereof a first compound selected from (1) triarylethylenes; (2)

2,3-diaryl-2H-1-benzopyrans, (3) 1-aminoalkyl-2-phenylindoles; (4) 2-phenyl-3-aroylbenzothiophenes, (5) 1-substituted-2-aryl-dihydronaphthalenes; of (6) benzofurans, and a second compound being a bisphosphonate or pharmaceutically acceptable salts and solvates thereof. Combination of 0.1 mg/kg raloxifene and 0.1 mg/kg alendronate demonstrated the greatest protection from bone loss in post-menopausal osteoporosis model in rats with the lowest exposure to the potentially undesirable side-effects of alendronate. Pharmaceutical formulations containing above combination are disclosed.

IT 129318-43-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing bisphosphonates and anti-resorptive agents for inhibiting bone loss)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



L16 ANSWER 24 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:163909 HCAPLUS
DOCUMENT NUMBER: 124:202606
TITLE: Process for recovery and recycle of methanesulfonic acid and phosphorous acid during manufacture of alendronate sodium, an agent for preventing bone resorption
INVENTOR(S): Venkataramani, Edamanal S.; Forman, Andrew L.; Magliette, Ralph J., Jr.; Vaughn, William A.; Dauer, Richard R.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9533756	A1	19951214	WO 1995-US6965	19950602 <--
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5589691	A	19961231	US 1994-254213	19940606 <--
AU 9526608	A	19960104	AU 1995-26608	19950602 <--
BR 9507921	A	19970923	BR 1995-7921	19950602 <--
CN 1164857	A	19971112	CN 1995-194515	19950602 <--

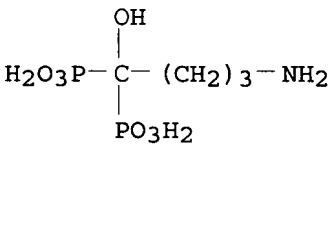
CN 1061048	B	20010124			
RU 2152950	C1	20000720	RU 1997-100188		19950602
RO 116281	B1	20001229	RO 1996-2297		19950602
SK 281212	B6	20010118	SK 1996-1579		19950602
CZ 289980	B6	20020515	CZ 1996-3545		19950602
FI 9604896	A	19970205	FI 1996-4896		19961205 <--
CN 1291607	A	20010418	CN 1999-126470		19991215
PRIORITY APPLN. INFO.:			US 1994-254213	A1	19940606
			WO 1995-US6965	W	19950602

AB Waste methanesulfonic acid and phosphorous acid from a bisphosphonation process are recovered and recycled for reuse in the process. The waste crude mother liquor stream containing sodium methanesulfonate and sodium phosphate is treated with hydrochloric acid to obtain a hydrochloric acid concentration of ≥6N to precipitate sodium chloride, which is removed. The separated sodium chloride is washed with saturated aqueous sodium salt solution to removed residual methanesulfonic acid. The hydrochloric acid and water are removed the remaining waste by atmospheric distillation and the mixture of methanesulfonic acid and phosphorous acid remaining is separated and dehydrated by vacuum distillation for recycle. The substantially dry methanesulfonic acid and phosphorous acid, and previous HCl, can all be recycled back to the process for reuse.

IT 129318-43-0P, Alendronate sodium
RL: IMF (Industrial manufacture); PREP (Preparation)
(process for recovery and recycle of methanesulfonic acid and phosphorous acid during manufacture of alendronate sodium, an agent for preventing bone resorption)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



L16 ANSWER 25 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:138147 HCAPLUS
DOCUMENT NUMBER: 124:194355
TITLE: Osteogenesis promoters containing bisphosphonic acids
INVENTOR(S): Tsuchimoto, Masahiro; Azuma, Yoshiaki; Higuchi, Osamu; Sugimoto, Izuki; Hirata, Noriko; Seiki, Mamoru
PATENT ASSIGNEE(S): Teijin Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

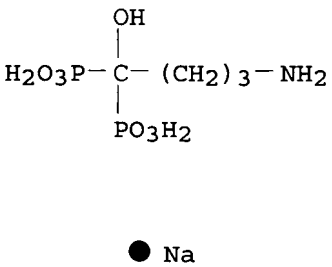
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07330613	A	19951219	JP 1994-121258	19940602 <--
JP 3566984	B2	20040915		
PRIORITY APPLN. INFO.:			JP 1994-121258	19940602
OTHER SOURCE(S):	MARPAT 124:194355			

AB Osteogenesis promoters containing HOCR(PO3H2)2 [R = (CH2)nNH2, Me; n = 2-5] or their salts as active ingredients are claimed. The promoters may be in the forms of oral prepns. or injections. Alendronate (I) at 10-12-10-7M significantly promoted calcification in human osteoblast-like cells cultured in the presence of 1α,25-dihydroxyvitamin D3 (II) and disodium α-glycerophosphate (III). I also promoted formation of osteocalcin and collagen by human osteoblast-like cells in the presence of II and III.

IT 129318-43-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteogenesis promoters containing bisphosphonic acids)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



L16 ANSWER 26 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:947515 HCAPLUS

DOCUMENT NUMBER: 124:117423

TITLE: Preparation of (4-Amino-1-Hydroxybutylidene)bisphosphonic Acid Sodium Salt, MK-217 (Alendronate Sodium). An Improved Procedure for the Preparation of 1-Hydroxy-1,1-bisphosphonic Acids

AUTHOR(S): Kieczykowski, Gerard R.; Jobson, Ronald B.; Melillo, David G.; Reinhold, Donald. F.; Grenda, Victor J.; Shinkai, Ichiro

CORPORATE SOURCE: Merck Research Laboratories, Merck and Co. Inc., Rahway, NJ, 07065, USA

SOURCE: Journal of Organic Chemistry (1995), 60(25), 8310-12
CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

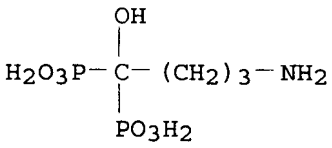
OTHER SOURCE(S): CASREACT 124:117423

AB Moderate to poor yields of 1-hydroxy-1,1-bisphosphonates, prepared by reacting a carboxylic acid with PCl3 and H3PO3, can be substantially increased by running the reaction in methanesulfonic acid. The target compds. thus prepared are (3-amino-1-hydroxypropylidene)bis[Phosphonic acid], (4-amino-1-hydroxybutylidene)bis[Phosphonic acid], etc., and alendronate sodium.

IT 129318-43-0P, Alendronate sodium
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of (aminohydroxybutylidene)bisphosphonates)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



● Na

L16 ANSWER 27 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:854365 HCAPLUS
DOCUMENT NUMBER: 123:265312
TITLE: Process for removing waste POx, alendronate and its byproducts from wastewaters for recycling as fertilizer
INVENTOR(S): Venkataramani, Edamanal S.; Forman, Andrew L.; Magliette, Jr Ralph J.; Mckinney, Donald
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5449819	A	19950912	US 1994-254805	19940606 <--
CA 2191772	A1	19951214	CA 1995-2191772	19950602 <--
WO 9533755	A1	19951214	WO 1995-US6964	19950602 <--
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9526607	A	19960104	AU 1995-26607	19950602 <--
AU 686819	B2	19980212		
EP 765332	A1	19970402	EP 1995-921572	19950602 <--
EP 765332	B1	19991215		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
HU 76709	A2	19971028	HU 1996-3360	19950602 <--
BR 9507932	A	19971118	BR 1995-7932	19950602 <--
RU 2126415	C1	19990220	RU 1997-100167	19950602
AT 187730	T	20000115	AT 1995-921572	19950602
ES 2141942	T3	20000401	ES 1995-921572	19950602
PT 765332	T	20000531	PT 1995-921572	19950602
SK 281649	B6	20010611	SK 1996-1578	19950602
CZ 289545	B6	20020213	CZ 1996-3546	19950602
RO 117614	B1	20020530	RO 1996-2296	19950602
HR 950319	B1	20001031	HR 1995-319	19950605
FI 9604895	A	19961205	FI 1996-4895	19961205 <--
GR 3032591	T3	20000531	GR 2000-400286	20000204

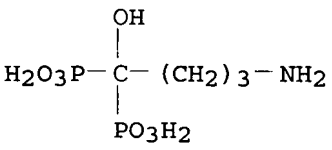
PRIORITY APPLN. INFO.: US 1994-254805 A 19940606
WO 1995-US6964 W 19950602

AB Byproducts P-containing (POx) materials, alendronate and alendronate byproducts are recovered from crude mother liquors in synthesis of an omega amino-1-hydroxy-C2-6-alkylidene-1,1-bisphosphonic acid, e.g. alendronate sodium. CaCl2 is added to the crude mother liquors, then CaO to precipitate the POx materials; then the liquor is neutralized to pH 7 for

complete precipitation Substantially all of the alendronate sodium active ingredient is removed from the precipitate Following filtration, the POx filter cake can be disposed of by incineration, landfilling or reclamation of usable P as fertilizer. The remaining filtrate can be further treated in an environmentally acceptable manner by wastewater treatment or recycling to the process.

IT 129318-43-0, Alendronate sodium
RL: NUU (Other use, unclassified); POL (Pollutant); REM (Removal or disposal); OCCU (Occurrence); PROC (Process); USES (Uses)
(removing waste POx, alendronate and its byproducts from wastewaters for recycling as fertilizer)

RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)

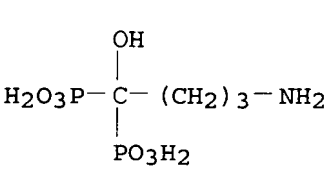


L16 ANSWER 28 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:827920 HCAPLUS
DOCUMENT NUMBER: 123:237995
TITLE: The determination of alendronate sodium in tablets by inductively coupled plasma (ICP)
AUTHOR(S): Reed, D. G.; Martin, G. P.; Konieczny, J. M.; Brooks, M. A.
CORPORATE SOURCE: Merck Research Laboratories, West Point, PA, 19486, USA
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (1995), 13(8), 1055-8
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

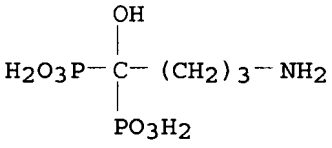
AB A rapid, precise, and accurate method was developed and validated for the determination of alendronate sodium in tablets.

IT 129318-43-0, Alendronate sodium
RL: ANT (Analyte); ANST (Analytical study)
(the determination of alendronate sodium in tablets by inductively coupled plasma (ICP))

RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



L16 ANSWER 29 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:502740 HCAPLUS
DOCUMENT NUMBER: 122:298947
TITLE: Development of subcutaneous and intramuscular formulations of calcium alendronate salts
AUTHOR(S): Ostovic, Drazen; Brenner, Gerald S.
CORPORATE SOURCE: Dep. Pharm. Res. Development, Merck Res. Lab., West Point, PA, 19486, USA
SOURCE: Drug Development and Industrial Pharmacy (1995), 21(10), 1157-69
CODEN: DDIPD8; ISSN: 0363-9045
PUBLISHER: Dekker
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Poorly soluble calcium alendronate salts were prepared and investigated as potential candidates for s.c. or i.m. formulations. Three such formulations containing calcium alendronate salts with different stoichiometries were developed for testing in safety, disposition and efficacy studies in animals. All formulations demonstrated a drastic reduction in pain on injection and tissue damaging propensity compared to the soluble salts of alendronate. All three were efficacious and showed prolonged absorption from the injection site with the deposition of a large percentage of the dose into the bone. Complex formation between alendronate and calcium was also studied.
IT 129318-43-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(s.c. and i.m. formulations of calcium alendronate)
RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



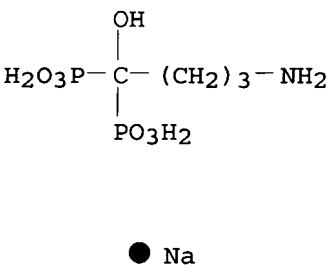
● Na

L16 ANSWER 30 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:478788 HCAPLUS
DOCUMENT NUMBER: 122:230528
TITLE: The diurnal rhythm of bone resorption in the rat: effect of feeding habits and pharmacological inhibitors
AUTHOR(S): Muehlbauer, Roman C.; Fleisch, Herbert
CORPORATE SOURCE: Dep. Pathophysiology, Univ. Berne, Bern, CH-3010, Switz.
SOURCE: Journal of Clinical Investigation (1995), 95(4), 1933-40
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Prevention of low bone mass is important to reducing the incidence of osteoporotic fractures. This paper shows that, in rats, bone mass can be increased by feeding habits per se. Using six-hourly urinary excretion of

[3H] tetracycline from prelabeled rats to monitor bone resorption, we previously found a peak of bone resorption following food administration. We now demonstrate that dividing the solid and liquid intake into portions blunts this peak and leads to a decrease in 24-h bone resorption to the level observed in thyroparathyroidectomized animals. Calcium balance increases and, when such feeding schedules are imposed for 30 d, bone mass increases. Dividing the intake is not effective in thyroparathyroidectomized animals, indicating the importance of PTH and/or calcitonin. Administration of calcitonin inhibits practically only the peak of bone resorption, suggesting that it is osteclast mediated. In contrast, treatment with a bisphosphonate reduces basal bone resorption without a specific effect on the peak, indicating a fundamentally different mechanism of action. This is also supported by the finding that their combined effects are additive. Whether bone mass in humans is also under the control of dietary habits is not known. If so, an increased meal frequency may be used to prevent osteoporosis.

IT 129318-43-0, Alendronate sodium
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diurnal rhythm of bone resorption in rat: effect of feeding habits and pharmacol. inhibitors)

RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)

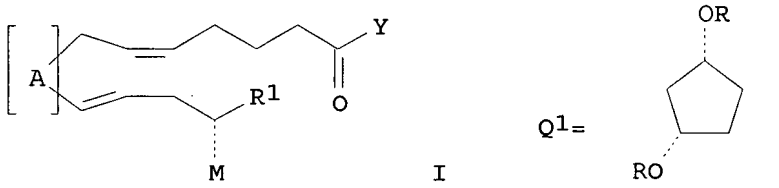


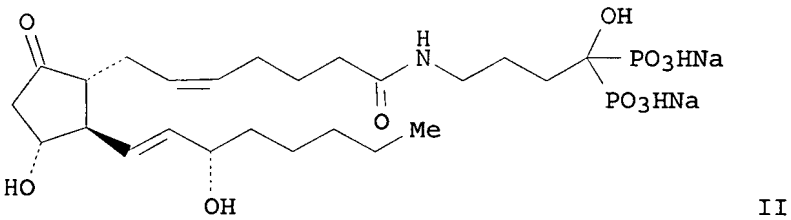
L16 ANSWER 31 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:408382 HCAPLUS
DOCUMENT NUMBER: 122:187237
TITLE: Preparation of prostaglandin derivatives for treating osteoporosis
INVENTOR(S): Tyler, Peter C.; Young, Robert N.; Rodan, Gideon A.; Ruel, Rejean
PATENT ASSIGNEE(S): Merck and Co., Inc., USA; Merck Frosst Canada Inc.
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9406750	A1	19940331	WO 1993-US8529	19930909 <--
W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5409911	A	19950425	US 1992-944149	19920911 <--
EP 662075	A1	19950712	EP 1993-921469	19930909 <--

EP 662075	B1	20011212			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
JP 08501546	T	19960220	JP 1993-508175	19930909	<--
AU 677597	B2	19970501	AU 1993-48554	19930909	<--
AU 9348554	A	19940412			
AT 210643	T	20011215	AT 1993-921469	19930909	
ES 2169046	T3	20020701	ES 1993-921469	19930909	
PRIORITY APPLN. INFO.:			US 1992-944149	A2 19920911	
			WO 1993-US8529	W 19930909	

OTHER SOURCE(S): MARPAT 122:187237
GI





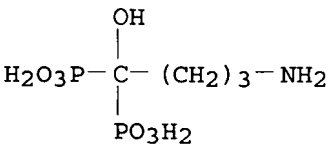
II

AB The title compds. I [A = Q1, etc.; R = H, SiMe2Bu-tert, etc.; R1 = H, alkyl; M = OH, OC1-6alkyl, etc.; Y = NH(CH2)nC(OH)(PO3H2)2, etc.; a proviso is given; n = 0 - 10] are prepared Prostaglandin derivative II was prepared from prostaglandin E2. Radioactive II (tritiated and 14C-labeled) was also prepared for biol. testing. In a test on the effect of radioactive II on bone resorption estimated by urinary excretion of lysylpyridinoline in the rat, animals treated with radioactive II had significantly lower levels of lysylpyridinoline after a 12 day period compared to vehicle alone.

IT 134606-40-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of prostaglandin derivs. for treatment of osteoporosis)

RN 134606-40-9 HCAPLUS

CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt (9CI) (CA INDEX NAME)

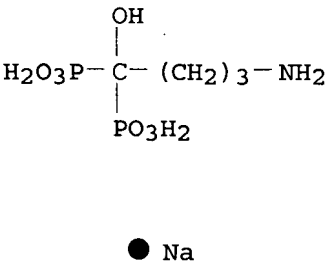


L16 ANSWER 32 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:232239 HCAPLUS
DOCUMENT NUMBER: 122:64540
TITLE: Pharmaceutical application of liquid chromatography-mass spectrometry. II. Ion chromatography-ion spray mass spectrometric characterization of alendronate
AUTHOR(S): Qin, Xue-Zhi; Tsai, Eric W.; Sakuma, Takeo; Ip, Dominic P.
CORPORATE SOURCE: Pharmaceutical Research and Development, Merck Research Laboratories, West Point, PA, 19486, USA
SOURCE: Journal of Chromatography, A (1994), 686(2), 205-12
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The trihydrate of alendronate sodium (MK-0217) is an important bisphosphonate drug for the treatment of a variety of bone diseases. Determination and characterization of this compound in dosage formulations is challenging since it has no chromophore, and as a highly polar and thermally labile compound, it is not amenable to electron impact mass spectrometry. Ion chromatog. coupled with an ion spray mass detector (IC-ISP-MS) in the neg. ionization mode was developed and applied to the characterization of this compound Under these conditions alendronate (m/z 248, [M-H]-, M = parent alendronic acid) was readily observed The anion can form cluster anions with acid mols. including that of the alendronic acid in the gas phase, which is a distinguishing feature of the IC-ISP-MS spectrum. IC-ISP-MS-MS study of the anion shows that cleavage of the C-P bond(s) is the dominant fragmentation pathway(s) of the anion, characteristic of its structure.

IT 129318-43-0, MK-0217
RL: ANT (Analyte); ANST (Analytical study)
(alendronate determination by ion chromatog.-ion spray mass spectrometry)
RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



● Na

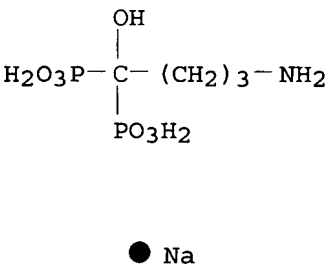
L16 ANSWER 33 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:426159 HCAPLUS
DOCUMENT NUMBER: 121:26159
TITLE: Use of Everted Intestinal Rings for in vitro Examination of Oral Absorption Potential
AUTHOR(S): Leppert, Paula S.; Fix, Joseph A.
CORPORATE SOURCE: Merck Research Laboratories, INTERx Research Corporation, Lawrence, KS, 66046, USA
SOURCE: Journal of Pharmaceutical Sciences (1994), 83(7), 976-81
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The ability to predict in vivo oral absorption potential based on ex vivo screening in an everted intestinal ring model was examined In vitro drug accumulation in cross sectional rings of everted rat jejunum was determined with 12 compds. whose in vivo absorptions (as distinct from bioavailabilities) are well characterized. The compds. examined ranged from well- to poorly-absorbed and included compds. absorbed by active and passive mechanisms. The effects of drug concentration, pH, cosolvents, and tissue origin site on drug accumulation were determined Light microscopic observation indicated that the mucosal tissue remained intact ≤3 h after the intestine was excised. Accumulations of two nonabsorbable markers were also determined as measures of tissue integrity. A strong correlation (slope = 23 pmol/mg of tissue weight per percent oral absorption, r2 = 0.9430 by linear regression anal.) of in vitro uptake into everted rings from a 10 mM drug solution vs. the known in vivo bioavailability for each compound was observed These results indicated that under appropriate conditions, in vitro uptake of drug by the everted intestinal ring model closely paralleled known in vivo bioavailability and was relatively independent of pH, cosolvent, and tissue origin.

IT 129318-43-0, MK-217
RL: BIOL (Biological study)
(absorption of, by intestine, everted jejunum rings of rat for evaluation of)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



L16 ANSWER 34 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:265154 HCAPLUS
DOCUMENT NUMBER: 120:265154
TITLE: Monitoring bone in early postmenopausal women by an immunoassay for cross-linked collagen peptides in urine
AUTHOR(S): Gertz, B. J.; Shao, P.; Hanson, D. A.; Quan, H.; Harris, S. T.; Genant, H. K.; Chesnut, C. H., III; Eyre, D. R.
CORPORATE SOURCE: Merck Res. Lab., Rahway, NJ, USA
SOURCE: Journal of Bone and Mineral Research (1994), 9(2), 135-42
CODEN: JBMREJ; ISSN: 0884-0431
DOCUMENT TYPE: Journal
LANGUAGE: English

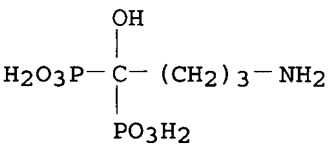
AB A new immunoassay using an ELISA approach for measuring urinary excretion of cross-linked N-telopeptides of type 1 collagen was evaluated as a specific measure of bone resorption. The assay was applied to 65 early postmenopausal women who participated in a placebo-controlled trial of the aminobisphosphonate, alendronate sodium. Eight blood and urine samples were collected over a 9 mo interval. Baseline cross-linked peptide excretion varied from 26 to 216 pmol BCE (bone collagen equivalent)/μmol Cr. Within-subjects, substantially less than that observed for other biochem. markers of bone resorption: 45, 53, and 63% for fasting urinary

calcium and hydroxyproline and 24 h urinary lysylpyridinoline (HPLC assay), resp. Baseline cross-linked peptide excretion correlated significantly with baseline total using lysylpyridinoline and serum osteocalcin, but not with the other biochem. markers. Initial peptide excretion also correlated inversely with lumbar spine bone mineral d. at entry (r = -0.26). Treatment for 6 wk with alendronate produced a dose-dependent suppression of cross-linked peptide excretion (0,29,56, and 64% for 0, 5, 20 and 40 mg, resp., vs. placebo for treatment effect), with a return toward pretreatment values during follow-up. Measurement of the urinary cross-linked N-telopeptides of type I collagen by this new ELISA approach appears promising as a simple and reliable method to assess overall bone resorption. It may prove especially useful in monitoring the treatment of osteoporotic women with antiresorptive therapy. Its utility in identifying those women in the high resorption range at menopause who may be at greater risk for osteoporosis should also be assessed in future studies.

IT 129318-43-0
RL: ANST (Analytical study)
(bone resorption in post-menopause women response to, ELISA assay in characterization of)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



● Na

L16 ANSWER 35 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:651559 HCAPLUS
DOCUMENT NUMBER: 117:251559
TITLE: Preparation of ω-(acylamino)alkylidenehydroxydiphosphonates for treatment of osteoarticular disease
INVENTOR(S): Rosini, Sergio; Mian, Maurizio
PATENT ASSIGNEE(S): Istituto Gentili S.p.A., Italy
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9213864	A1	19920820	WO 1992-EP102	19920120 <--
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
AU 9211709	A	19920907	AU 1992-11709	19920120 <--
AU 653780	B2	19941013		
EP 569411	A1	19931118	EP 1992-903398	19920120 <--
EP 569411	B1	19950329		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				

HU 64964	A2	19940328	HU 1993-2188		19920120 <--
HU 215918	B	19990329			
JP 06504783	T	19940602	JP 1992-503474		19920120 <--
JP 3046624	B2	20000529			
RU 2079505	C1	19970520	RU 1993-52408		19920120 <--
SK 280053	B6	19990712	SK 1993-799		19920120
HU 217588	B	20000228	HU 1998-1273		19920120
CZ 288731	B6	20010815	CZ 1993-1533		19920120
CA 2101548	C	20020827	CA 1992-2101548		19920120
FI 105403	B1	20000815	FI 1993-3231		19930716
US 5466682	A	19951114	US 1993-94160		19930726 <--
PRIORITY APPLN. INFO.:			IT 1991-MI254	A	19910201
			HU 1993-2188	A	19920120
			WO 1992-EP102	A	19920120

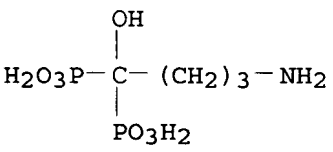
OTHER SOURCE(S): MARPAT 117:251559

AB RNHAC(OH)(PO3H2) [A = (CH2)n; n = 1-10; R = acyl residue from an antiinflammatory of the salicylate, arylacetate, arylpropionate, anthranilate, nicotinate, or hydroxydihydrodioxoanthracenecarboxylate classes] were prepared Thus, H2N(CH2)3C(OH)(PO3H2)2 mono-Na salt, NaOH, p-dimethylaminopyridine, and tetrahexylammonium iodide in H2O at 0° were treated with 2-AcOC6H4COCl in Et2O and the mixture was stirred 2 h at room temperature to give 2-AcOC6H4CONH(CH2)3C(OH)(PO3H2)2. Title compds. gave 32.4-73.9% inhibition of retinoid-induced bone Ca loss in rats. I show higher antiinflammatory activity than would be expected for simple prodrugs of the corresponding acids ROH, e.g., ibuprofen.

IT 129318-43-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation of, in preparation of drug for treatment of osteoarticular disease)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



Na

L16 ANSWER 36 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1992:531383 HCAPLUS

DOCUMENT NUMBER: 117:131383

TITLE: Preparation of amino(hydroxy)alkylidenebisphosphonic acids

INVENTOR(S): Kieczykowski, Gerard R.

PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: Brit. UK Pat. Appl., 19 pp.
CODEN: BAXXDU

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2248061	A	19920325	GB 1991-19201	19910909 <--

US 5159108	A	19921027	US 1991-742142		19910801 <--
PRIORITY APPLN. INFO.:			US 1990-584318	A	19900918

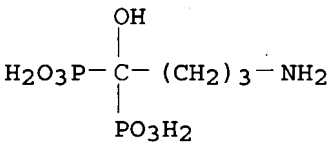
OTHER SOURCE(S): CASREACT 117:131383

AB A process for producing ω-amino-1-hydroxybutylidene-1, 1-bisphosphonic acids (e.g. ABP), useful as antihypercalcemic agents, involves a 3-step sequence starting with 4-phthalimidobutanoyl chloride which can be practiced as a "one-pot" reaction sequence, without employing PCl3 or H3PO3. Intermediates in the process are dialkyl ω-phthalimidoalkanoylphosphonates and tetraalkyl ω-phthalimido-1-hydroxy alkylidenebisphosphonates.

IT 129318-43-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antihypercalcemic activity of)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



● Na

L16 ANSWER 37 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

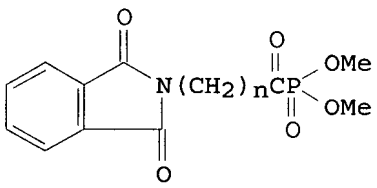
ACCESSION NUMBER:	1992:426807 HCAPLUS
DOCUMENT NUMBER:	117:26807
TITLE:	Preparation of phthalimidoalkanoylphosphonates as intermediates for (aminohydroxyalkylidese)bisphosphonates
INVENTOR(S):	Kieczykowski, Gerard R.
PATENT ASSIGNEE(S):	Merck and Co., Inc., USA
SOURCE:	Brit. UK Pat. Appl., 18 pp. CODEN: BAXXDU
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
GB 2248063	A	19920325	GB 1991-19223		19910909 <--
PRIORITY APPLN. INFO.:			US 1990-584310	A	19900918

OTHER SOURCE(S): MARPAT 117:26807

GI



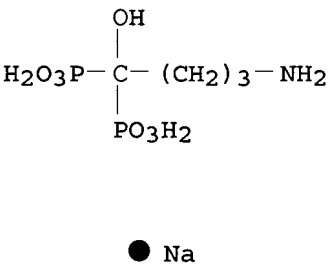
I

AB Title compds. (I; n = 1-5), were prepared as intermediates for 4-amino-1-hydroxyalkylidene-1,1-bisphosphonic acids. Thus, H2N(CH2)3CO2H, phthalic anhydride, and HOAc were refluxed 2 h to give 93% 4-phthalimidobutanoic acid, which was stirred with SOCl2 in PhMe at 45-50° to give the acid chloride. This was stirred with P(OMe)3 in PhMe at 20-25° to give I (n = 3). The latter was converted to (4-amino-1-hydroxybutylidene)bisphosphonic acid monosodium salt.

IT 129318-43-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



L16 ANSWER 38 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:670695 HCAPLUS
DOCUMENT NUMBER: 115:270695
TITLE: Use of bisphosphonic acid calcium salts for the treatment of calcium metabolism disorders
INVENTOR(S): Brenner, Gerald S.; Ostovic, Drazen
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 449405	A2	19911002	EP 1991-300740	19910130 <--
EP 449405	A3	19921021		
EP 449405	B1	19980812		
R: CH, DE, FR, GB, IT, LI, NL				
CA 2035179	A1	19910801	CA 1991-2035179	19910129 <--
CA 2035179	C	20010814		
JP 04211015	A	19920803	JP 1991-10556	19910131 <--
JP 3033783	B2	20000417		
US 5356887	A	19941018	US 1993-118832	19930907 <--

PRIORITY APPLN. INFO.:
US 1990-472987 A 19900131
US 1990-561026 A 19900801
US 1991-714467 B1 19910613
US 1992-924432 B1 19920731

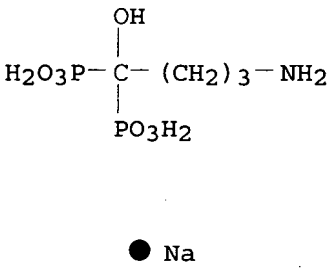
AB An insol. bisphosphonic acid Ca salt, e.g. di[4-amino-1-hydroxybutylidene)-1,1-bisphosphonic acid] monocalcium salt (I), is formulated into an aqueous suspension for i.m. and s.c. administration in the prevention or treatment of Ca metabolism disturbances. The Ca salts provide a slow systemic release of the bisphosphonic acid and reduce tissue damage and localized pain and irritation. Thus, I was suspended in a vehicle containing Na CMC, NaCl, NaOc, and distilled water. S.c. administration of the suspension of I to rats

exhibited a lower tendency to induce irritation at the site of injection, compared to the solution of [(4-amino-1-hydroxybutylidene)-1,1-bisphosphonic acid] Na salt (II), and the bone loss in rats undergoing immobilization surgery was less than the control group treated with II.

IT 129318-43-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and conversion of, to calcium salt)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)

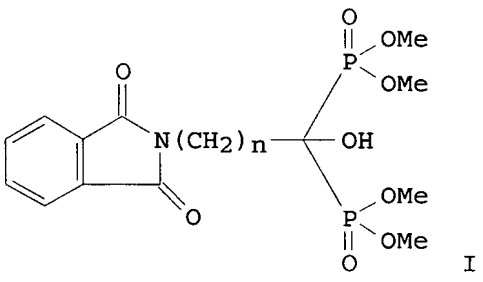


L16 ANSWER 39 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:583588 HCAPLUS
DOCUMENT NUMBER: 115:183588
TITLE: Preparation of tetramethyl ω-phthalimido-1-hydroxyalkylidenebisphosphonates as intermediates for antihypercalcemics
INVENTOR(S): Kieczykowski, Gerard R.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5039819	A	19910813	US 1990-584322	19900918 <--
GB 2248062	A	19920325	GB 1991-19221	19910909 <--

PRIORITY APPLN. INFO.: US 1990-584322 A 19900918
OTHER SOURCE(S): CASREACT 115:183588
GI



I

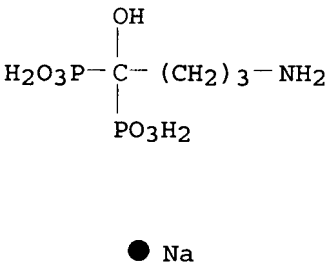
AB Title compds. (I; n = 1-5), were prepared H2N(CH2)3 CO2H was refluxed with phthalic anhydride in HOAc to give 91.8% 4-phthalimidobutanoic acid, which

was converted in situ to the acid chloride in PhMe solution The solution was treated with (MeO)3P and then (MeO)2P(O)H to give 92% I (n = 3). The latter was refluxed with 6N HCl to give, H2N(CH2)3C(OH)(PO3H2)2.

IT 129318-43-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, via tetra-Me phthalimidohydroxybutylidene bisphosphonate)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



L16 ANSWER 40 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:559444 HCAPLUS
DOCUMENT NUMBER: 115:159444
TITLE: Process for preparing 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid (ABP) or salts thereof
INVENTOR(S): Kieczykowski, Gerard R.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 4 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5019651	A	19910528	US 1990-540997	19900620 <--
IL 98462	A	19951208	IL 1991-98462	19910612 <--
EP 462663	A1	19911227	EP 1991-201490	19910614 <--
EP 462663	B1	19950927		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 128470	T	19951015	AT 1991-201490	19910614 <--
ES 2079026	T3	19960101	ES 1991-201490	19910614 <--
CA 2044923	A1	19911221	CA 1991-2044923	19910618 <--
CA 2044923	C	19960618		
AU 9178498	A	19920102	AU 1991-78498	19910618 <--
AU 642264	B2	19931014		
FI 9103008	A	19911221	FI 1991-3008	19910619 <--
FI 94347	B	19950515		
FI 94347	C	19950825		
NO 9102395	A	19911223	NO 1991-2395	19910619 <--
NO 180050	B	19961028		
NO 180050	C	19970205		
ZA 9104708	A	19920325	ZA 1991-4708	19910619 <--
JP 05132492	A	19930528	JP 1991-147090	19910619 <--
JP 07119229	B	19951220		
RO 112355	B1	19970829	RO 1992-1582	19921218 <--
LV 11471	B	19961220	LV 1996-27	19960202 <--

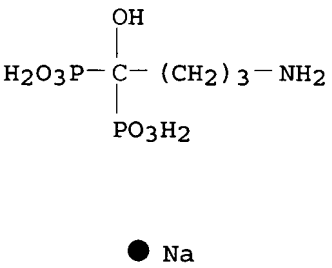
PRIORITY APPLN. INFO.: US 1990-540997 A 19900620
OTHER SOURCE(S): CASREACT 115:159444

AB An improved process is described for the preparation of 4-amino-1-hydroxybutylidene-1,1-bisophosphonic acid or salts thereof which comprises: (a) reacting 4-aminobutyric acid with a mixture of phosphorous acid and PCl3 in the presence of methanesulfonic acid; (b) contacting the mixture from Step (a) with an aqueous hydrolysis mixture, wherein the pH is maintained in the range of 4 to 10 during the contacting; and (c) recovering said 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid or salts thereof.

IT 129318-43-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



L16 ANSWER 41 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:464499 HCAPLUS

DOCUMENT NUMBER: 115:64499

TITLE: The bisphosphonate alendronate (MK-217) inhibits bone loss due to ovariectomy in rats

AUTHOR(S): Seedor, J. Gregory; Quartuccio, Helen A.; Thompson, David D.

CORPORATE SOURCE: Dep. Bone Biol. Osteoporosis Res., Merck, Sharp and Dohme Res. Lab., West Point, PA, 19486, USA

SOURCE: Journal of Bone and Mineral Research (1991), 6(4), 339-46
CODEN: JBMREJ; ISSN: 0884-0431

DOCUMENT TYPE: Journal

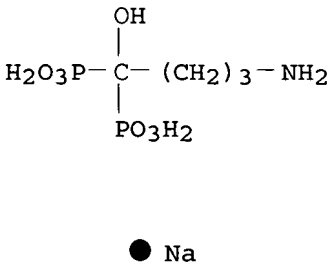
LANGUAGE: English

AB Estrogen deficiency in mammals is known to increase bone turnover and result in reduced bone mass. The bisphosphonate, 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid disodium salt, alendronate (MK-217), is a potent inhibitor of bone resorption and was evaluated in this study for its ability to inhibit bone loss following ovariectomy in rats. Alendronate (MK-217) was effective in inhibiting bone loss due to estrogen deficiency in rats, and the magnitude of its effect was related primarily to the total amount of compound administered rather than the frequency of its administration.

IT 129318-43-0, MK-217
RL: BIOL (Biological study)
(bone resorption inhibition by, after ovariectomy)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



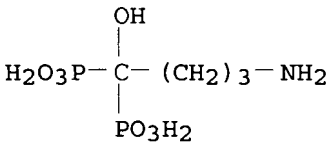
L16 ANSWER 42 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:429628 HCAPLUS
DOCUMENT NUMBER: 115:29628
TITLE: Preparation of acyloxymethyl esters of bisphosphonic acids as bone resorption inhibitors
INVENTOR(S): Saari, Walfred S.; Anderson, Paul S.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 416689	A2	19910313	EP 1990-202312	19900829 <--
EP 416689	A3	19910626		
EP 416689	B1	19951129		
R: CH, DE, FR, GB, IT, LI, NL				
US 5227506	A	19930713	US 1990-549497	19900712 <--
CA 2024694	A1	19910307	CA 1990-2024694	19900905 <--
CA 2024694	C	20001017		
JP 03106893	A	19910507	JP 1990-234649	19900906 <--
JP 07119230	B	19951220		
LV 11473	B	19961220	LV 1996-33	19960206 <--
PRIORITY APPLN. INFO.:			US 1989-403411 A	19890906
OTHER SOURCE(S):	MARPAT 115:29628			

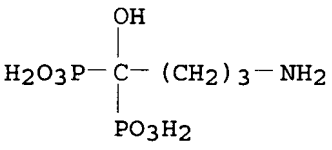
AB (YO)2P(O)CRR1P(O)(OY)OCH2O2CR2 [R = H, halo, OH; R1 = (substituted) alkyl, cycloalkyl, halo, piperidinyl, pyrrolidinyl, alkylthio, PhS; R2 = alkyl; Y = H, CH2O2CR2] were prepared Thus, H2N(CH2)3C(PO3H2)2OH di-Na salt in THF/H2O was treated with PhCH2O2CCl to give 66% PhCH2O2CNH(CH2)3C(PO3H2)OH. The latter was treated with ClCH2O2CCMe3 and (Me2CH)2NEt in DMF to give a separable mixture of di- and triesters. The diester was hydrogenolyzed in EtOH over Pd/C to give H2N(CH2)3C(PO3H2)2OH di(pivaloyloxymethyl) ester. The latter at 0.5 mg/kg s.c. in rats reduced immobilization-induced hind limb bone loss from 27.6 mg (controls) to 7.3 mg.

IT 129318-43-0 134606-40-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of bone resorption inhibitor)

RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)

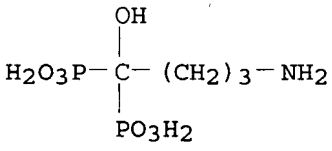


RN 134606-40-9 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt (9CI) (CA INDEX NAME)



L16 ANSWER 43 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:12304 HCAPLUS
DOCUMENT NUMBER: 114:12304
TITLE: HPLC analysis of an amino bisphosphonate in pharmaceutical formulations using postcolumn derivatization and fluorescence detection
AUTHOR(S): Kwong, E.; Chiu, A. M. Y.; McClintock, Sam A.; Cotton, M. L.
CORPORATE SOURCE: Merck Frosst Cent. Ther. Res., Pointe Claire-Dorval, QC, H9R 4P8, Can.
SOURCE: Journal of Chromatographic Science (1990), 28(11), 563-6
CODEN: JCHSBZ; ISSN: 0021-9665
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Monosodium 4-amino-1-hydroxybutane-1,1-diphosphonic acid (MK-217) is a bone resorption inhibitor implicated in the treatment of malignant hypercalcemia. This compound is very water soluble and has five ionizable groups with pKa values over the entire pH range. As a result, it is difficult to maintain a single species in solution for chromatog. separation Since there is no chromophore in the mol. structure, UV detection is ineffective. The compound and its potential degradation products are separated by ion-pair chromatog. using 0.01M cetyltrimethylammonium bromide as the ion-pairing agent and a polymeric stationary phase. Detection is by fluorescence detection after postcolumn derivatization of the primary amine with o-phthalaldehyde and mercaptoethanol (OPA-MERC). Optimization of the chromatog. separation and the postcolumn reaction has been carried out, and the method was applied to the anal. of MK-217 in i.v. solns. and tablet formulations.
IT 129318-43-0, MK 217
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in pharmaceuticals by HPLC, postcolumn derivatization and fluorescence detection in)
RN 129318-43-0 HCAPLUS
CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1)

(CA INDEX NAME)



● Na

L16 ANSWER 44 OF 44 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:532508 HCAPLUS
DOCUMENT NUMBER: 113:132508
TITLE: Process for preparing 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid or salts thereof
INVENTOR(S): Kieczykowski, Gerard R.; Melillo, David G.; Jobson, Ronald B.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 3 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 4922007	A	19900501	US 1989-363820	19890609	<--
IL 94612	A	19950330	IL 1990-94612	19900604	<--
CA 2018477	A1	19901209	CA 1990-2018477	19900607	<--
CA 2018477	C	19950801			
FI 93219	B	19941130	FI 1990-2845	19900607	<--
FI 93219	C	19950310			
NO 9002559	A	19901210	NO 1990-2559	19900608	<--
NO 177997	B	19950925			
NO 177997	C	19960103			
EP 402152	A2	19901212	EP 1990-306238	19900608	<--
EP 402152	A3	19910703			
EP 402152	B1	19951102			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
AU 9057019	A	19901213	AU 1990-57019	19900608	<--
AU 625704	B2	19920716			
ZA 9004446	A	19920624	ZA 1990-4446	19900608	<--
AT 129713	T	19951115	AT 1990-306238	19900608	<--
ES 2080116	T3	19960201	ES 1990-306238	19900608	<--
KR 137455	B1	19980501	KR 1990-8394	19900608	<--
JP 03101684	A	19910426	JP 1990-152494	19900611	<--
JP 06062651	B	19940817			
JP 07048391	A	19950221	JP 1994-34560	19940304	<--
NO 9401726	A	19901210	NO 1994-1726	19940509	<--
NO 178228	B	19951106			
NO 178228	C	19960214			
LV 11472	B	19961220	LV 1996-28	19960202	<--

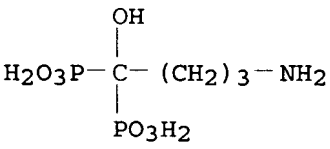
PRIORITY APPLN. INFO.: US 1989-363820 A 19890609
NO 1990-2559 A 19900608
OTHER SOURCE(S): CASREACT 113:132508
AB The title compound (I) is prepared by a 1-pot procedure in a particularly pure form and high yield by reacting H2N(CH2)3CO2H with a mixture of H3PO3 and

PCl3 in the presence of MeSO3H. I mono-Na salt is useful as a pharmaceutical for treatment or prevention of diseases involving bone resorption (no data). H2N(CH2)3CO2H, MeSO3H, and H3PO3 were mixed (exothermic to 75°) and the mixture was heated at 70-75°, cooled to 35°, and treated cautiously with PCl3 over 20 min. The mixture was kept for 20 h at 65°, being ready to quench into cold H2O if the temperature reached 85° (prevents self-heating to dangerous exotherm at 150°). After cooling, addition to H2O, heating at 95-100°, and cooling, the pH was adjusted to 4.3 with NaOH to give I mono-Na salt in 90% yield. Adjusting the pH to 1.8 instead gave I in 86% yield.

IT 129318-43-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for treatment of bone resorption disease)

RN 129318-43-0 HCAPLUS

CN Phosphonic acid, P,P'-(4-amino-1-hydroxybutylidene)bis-, sodium salt (1:1) (CA INDEX NAME)



Na

```
=> s alendronate
L13          9 ALENDRONATE

=> d l13

L13  ANSWER 1 OF 9  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   548457-56-3  REGISTRY
ED   Entered STN:  15 Jul 2003
CN   Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, calcium salt (9CI)
     (CA INDEX NAME)
OTHER NAMES:
CN   Calcium alendronate
MF   C4 H13 N O7 P2 . x Ca
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPATFULL
CRN  (66376-36-1)
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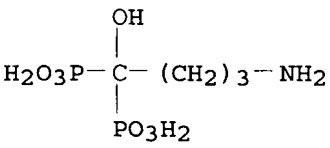


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             x  Ca

             3 REFERENCES IN FILE CA (1907 TO DATE)
             3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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L13  ANSWER 2 OF 9  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   260055-05-8  REGISTRY
ED   Entered STN:  27 Mar 2000
CN   Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt,
     monohydrate (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Alendronate monosodium monohydrate
CN   MonoSodium Alendronate monohydrate
MF   C4 H13 N O7 P2 . H2 O . Na
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
CRN  (66376-36-1)
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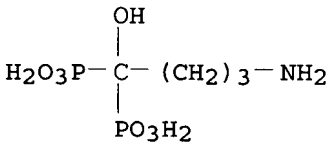
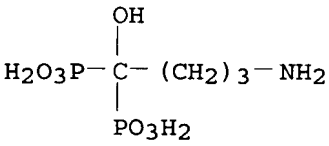


17 REFERENCES IN FILE CA (1907 TO DATE)
17 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 3 OF 9 REGISTRY COPYRIGHT 2007 ACS on STN
RN 185960-02-5 REGISTRY
ED Entered STN: 11 Feb 1997
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, hydrate (2:1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Disodium alendronate hemihydrate
MF C4 H13 N O7 P2 . 1/2 H2 O . 2 Na
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
CRN (66376-36-1)

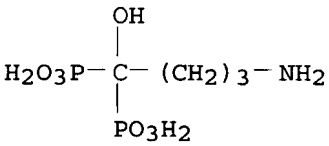


●2 Na

●1/2 H_2O

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 4 OF 9 REGISTRY COPYRIGHT 2007 ACS on STN
RN 185960-00-3 REGISTRY
ED Entered STN: 11 Feb 1997
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, trihydrate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Disodium alendronate trihydrate
MF C4 H13 N O7 P2 . 3 H2 O . 2 Na
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
CRN (66376-36-1)

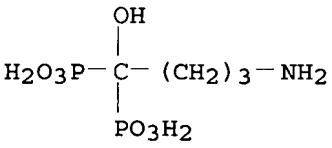


●2 Na

●3 H_2O

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 5 OF 9 REGISTRY COPYRIGHT 2007 ACS on STN
RN 185959-99-3 REGISTRY
ED Entered STN: 11 Feb 1997
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, pentahydrate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Disodium alendronate pentahydrate
MF C4 H13 N O7 P2 . 5 H2 O . 2 Na
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
CRN (66376-36-1)

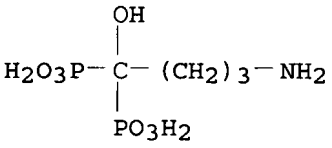


●2 Na

●5 H_2O

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 6 OF 9 REGISTRY COPYRIGHT 2007 ACS on STN
RN 185959-98-2 REGISTRY
ED Entered STN: 11 Feb 1997
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, monohydrate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Disodium alendronate monohydrate
MF C4 H13 N O7 P2 . H2 O . 2 Na
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
CRN (66376-36-1)



●2 Na

● H_2O